Gastrointestinal cancer screening and surveillance programmes: a worldwide perspective – Part II

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Stomach

Gastric cancer remains one of the most important malignant diseases with significant geographical differences in distribution. Annual mass screening for gastric cancer has been provided in Japan, Chile and Venezuela, aiming at detecting early gastric cancer. Japan introduced this screening programme in the 1960s using barium X-ray studies[6]. Barium X-ray study was regarded as a superior screening test out of four tests that were evaluated and studied, mainly photofluorography, serum pepsinogen levels, endoscopy and H. pylori antibody testing[7]. Sensitivity ranged between 60-80% and specificity ranged between 80-90%. Those that had an abnormal X-ray were offered upper endoscopy together with treatment. The 5 year survival rates that were achieved, as reported in 2008, were 74-80% in the screened group versus 46-56% in the non-screened group. Despite this programme, 40% of gastric cancers remain undetected and overall mortality was reduced by only 8%. This was mainly due to selection bias as the people who underwent screening were generally healthier than those who did not [6]. Moreover, a cohort of 24,000 individuals in Japan, classified into screened and unscreened groups and followed up for 40 months (1992 – 1995), failed to show statistically significant reduction in mortality, once again due to selection bias[8].

While gastric cancer screening is not practiced in the US, ASGE suggests carrying out surveillance endoscopy in patients with gastric premalignant conditions. Gastric adenomas have a high malignant potential and should be resected endoscopically or surgically with a surveillance endoscopy 1 year post-resection to assess the excision site, and every 3-5 years thereafter if the stomach is polyp-free. Patients with gastric intestinal metaplasia are not advised to undergo surveillance as there is lack of data in this field. On the other hand, patients with high grade dysplasia of the stomach should be considered for gastrectomy. Lastly, patients with FAP and tylosis should undergo surveillance programmes, while others with HNPCC should be considered for surveillance[9].

Small Bowel

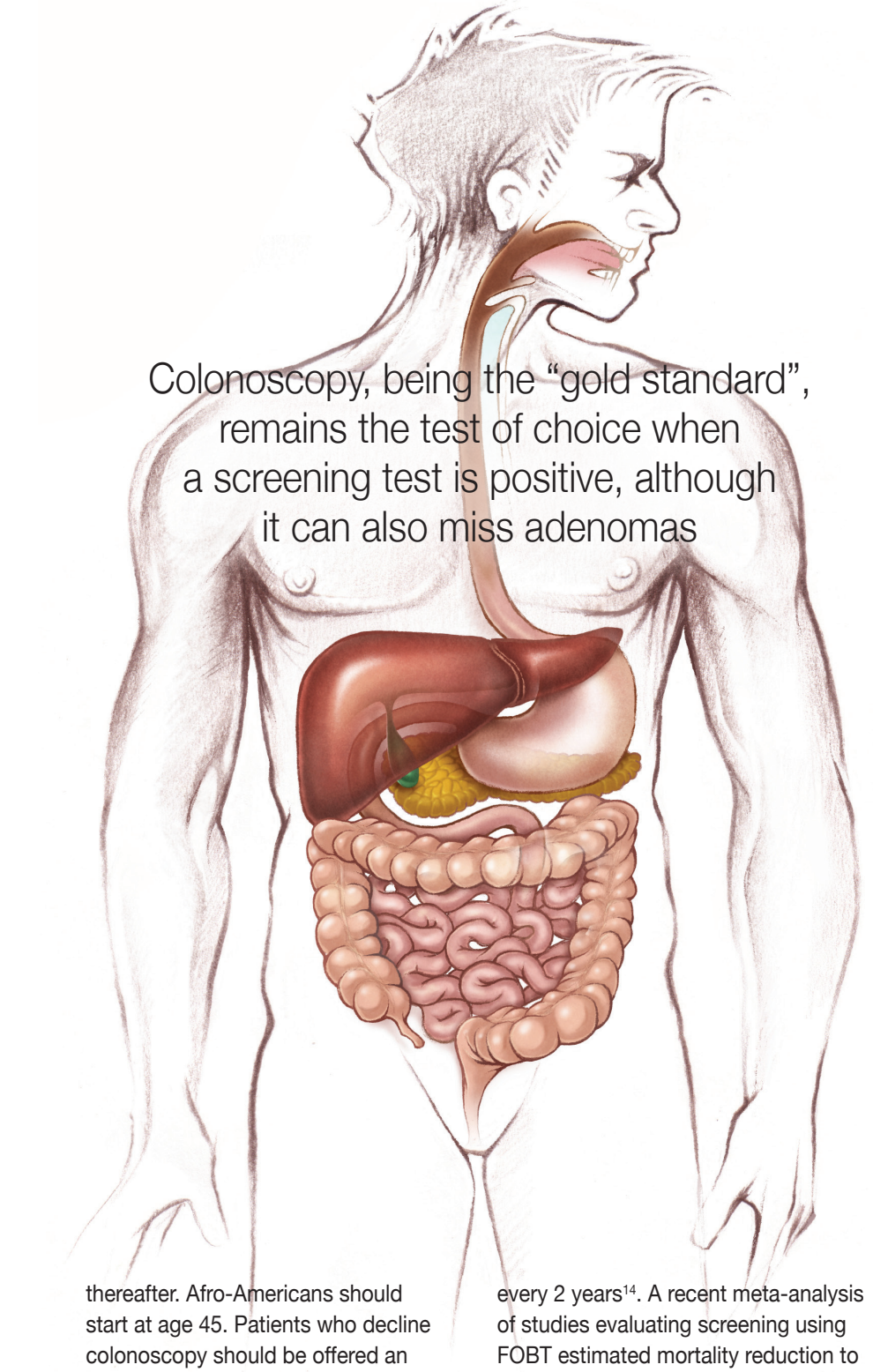
Tumors of the small bowel are quite rare and for this reason, there is a severe lack of guidelines on their management. To date, there are no screening programmes to detect small bowel tumors in asymptomatic individuals. Sporadic duodenal and ampullary adenomas are usually found incidentally during a routine OGD. These have been described to have malignant potential and ASGE has recommended surveillance post-surgical or endoscopic resection. Surveillance for ampullary neoplasms vary from 1-6 months after the index procedure, followed by a repeat exam every 3-12 months for a period of at least 2 years. High grade dysplastic lesions require more intense monitoring. Formal recommendations regarding surveillance intervals for duodenal adenomas, on the other hand, could not be given due to the limited data available and should be decided on an individual basis. Moreover, data suggest that patients with duodenal or ampullary neoplasms are at a higher risk of colorectal polyps and neoplasia and should be offered screening colonoscopy[10].

Colon

In 2002, CRC comprised 9.4% of the global cancer burden and its incidence is expected to increase as the world's population is ageing. The risk of CRC increases with age and family history. It is rare below the age of 50 but increases dramatically thereafter. CRC is the only gastrointestinal cancer where screening asymptomatic patients is practiced in many countries, with Malta joining them this October. CRC screening is however complex as there are multiple options and requires patient effort[11].

The two most common tests used for this screening are a stool-based test and an endoscopy or radiological-based test. Stool-based tests work on the basis that they detect blood shed by the tumor. The guaiac fecal occult blood test is the most common test used, however it requires dietary restrictions to avoid false positive results. Fecal immunochemical testing, on the other hand, obviates the need for these restrictions. Endoscopy, in the form of flexible sigmoidoscopy, is also widely practiced. This entails examination of the colon up to 60cm, is less time-consuming than a colonoscopy, avoids sedation, bowel preparation is easier and morbidity is negligible if polypectomy is not required. Therapeutic procedures in the same examination can also be done. The disadvantage is that it misses right-sided lesions. Colonoscopy, being the "gold standard", remains the test of choice when a screening test is positive, although it can also miss adenomas. Alternatively to endoscopy, in countries with limited resources, radiological tests such as DCBE or CT colonography remain a possibility. DCBE, although inferior to colonoscopy, may still detect 50% of large polyps. CT colonography, on the other hand, has high sensitivity and specificity for large polyps but less so for small polyps. Disadvantages include the fact that flat lesions are frequently missed and patients are exposed to ionized radiation[11].

Below, we shall see how screening is carried out differently in different countries. In the US, ACG recommends that quality colonoscopy is offered first, starting at age 50, and every 10 year



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thereafter. Afro-Americans should start at age 45. Patients who decline colonoscopy should be offered an annual fecal immunochemistry test or a 5-yearly flexible sigmoidoscopy[12]. A completely different approach is adopted in UK. Individuals between the ages 60 – 69 are invited for screening every 2 years. FOBTs are sent out by post to their home and thereafter every 2 years until age 69. This is done if the test is negative. Positive tests will then be followed up by a colonoscopy[13]. Scotland has a similar programme to that of the UK, however they have extended the age range from 50 – 74. A positive FOBT will be followed by a colonoscopy, whereas a negative FOBT will be followed up by a repeat FOBT every 2 years[14]. A recent meta-analysis of studies evaluating screening using FOBT estimated mortality reduction to be 15%[15].

Recent data suggests that 5 countries, namely UK, France, Australia, Belgium and Finland now offer national screening programmes, the most common screening modality being FOBT, followed up by endoscopy in positive tests. On the other hand, another 6 countries, namely US, Germany, New Zealand, Portugal, Switzerland and Spain, offer opportunistic screening where a test is offered to asymptomatic individuals who have seeked medical help for other reasons unrelated to CRC [15].

Patients with moderate or high risk of colorectal cancer

Patients who have a moderate or high risk of developing CRC are thus screened as part of a surveillance programme. Patients with moderate risk include patients with a positive family history of CRC, while patients with high risk include:

- Patients following detection of colorectal adenomas;
- Patients with inflammatory bowel disease;
- Patients following CRC resection;
- Patients with acromegaly;
- Patients with FAP, HNPCC, juvenile polyposis and peutz-jeghers syndrome;
- Patients with ureterosigmoidostomy.

It is worth mentioning some differences between US and UK regarding these programmes in the moderate risk group and the first 2 high risk groups:

Family History of Colorectal Cancer

Guidelines issued by the ACG in 2008 recommend patients with a first-degree relative diagnosed with CRC at age ≥60 years to have screening as the average risk population, i.e. colonoscopy every 10 years, starting age 50. Patients with a first-degree relative diagnosed with CRC or advanced adenomas at age <60 years, or two first-degree relatives with CRC or advanced adenomas, should have a colonoscopy every 5 years starting at age 40, or 10 years younger than the age of diagnosis of the youngest affected relative[12]. On the other hand, BSG guidelines, issued in 2010, recommend patients with one affected first-degree relative age <50, to have a single colonoscopy at age 55 and average risk population recommendations thereafter. If the first-degree relative was diagnosed age ≥50, recommendations are the same as the average risk population[16].

Patients with colorectal adenomas

2010 BSG guidelines risk-stratify such patients into low, intermediate or high risk depending on the number and size of adenomas detected. Surveillance is by means of colonoscopy every 5 years for low risk patients (1-2 adenomas, both <1cm), every 3 years for intermediate risk patients (3-4 small adenomas or at

least one ≥1cm) and every year for high risk patients (≥5 small adenomas or ≥3 at least ≥1cm)[16]. ASGE guidelines also stratify such patients in a similar way, the only difference being in the intermediate risk where the number of adenomas can be from 3 – 10[17].

Patients with inflammatory bowel disease

CRC surveillance in this high risk group using colonoscopy and pancolonic dye-spray should start after 10 years of colitic symptoms. Once again, BSG guidelines stratify patients in low, intermediate and high risk depending mainly on disease activity and extent and other risk factors such as FH of CRC or PSC. Low risk patients (no active disease) should repeat colonoscopy every 5 years, intermediate risk patients (mild active disease or FH) every 3 years and high risk patients (moderate/severe active disease or FH or PSC) every year[16]. On the other hand, ASGE recommends colonoscopy every one or two years beginning 8 – 10 years after disease onset in patients with extensive colitis. A case-control study showed a reduction in mortality in CRC in patients with ulcerative colitis using such surveillance programme[17].

Liver, biliary tree and pancreas

Surveillance for HCC is widely practiced across the world, however it is still controversial whether such management is beneficial or not, and which surveillance modality is best to use. In the US, the patients at risk of developing HCC, who are routinely surveilled, are

- Hepatitis B carriers: asian males over 40; asian females over 50; african/north american blacks; family history of HCC;
- All patients with cirrhosis.

The rationale for such surveillance is to detect small HCC lesions as these are amenable to resection or liver transplantation. AASLD, in 2010, recommended screening these patients with just an ultrasound every 6 months. They argue that AFP, having a sensitivity of 66% and a specificity of 82%, is still inadequate as a screening test for HCC[18].

In 2009, WGO suggested screening every 6-12 months in some patients, depending on the clinical scenario, whereas in high-risk patients, this should be done every 4-6 months. The test they recommend is an ultrasound, as the AFP still shows an imbalance between sensitivity and specificity. Moreover, combining both tests increased costs and false positive rates[19].

On the other hand, BSG in 2003, recommended 6-monthly screening using both AFP and ultrasound to the same at-risk population mentioned above. They emphasized the use of high quality ultrasound with a dedicated equipment and operator expertise. Despite these recommendations, they also stated that there is not enough data to show long-term improvement in survival with this programme[20]. Following these guidelines, a new randomized controlled trial, in 2004, carried out in China, comparing surveillance versus no surveillance, showed a reduction in mortality by 37% when 6-monthly surveillance strategy using AFP and ultrasound was applied[21].

As regards cholangiocarcinomas and pancreatic tumors, as of today, there are no screening programmes in asymptomatic patients.

Conclusion

Screening programmes are challenging and complex to organize. For these to be successful, multiple events have to occur hand-in-hand, starting from patient awareness and primary care physician recommendation, to patient acceptance, financial coverage, risk stratification, screening test, timely diagnosis, timely treatment to appropriate follow-up. If any of these is not of high quality, then screening will fail[11]. Although the above screening programmes are already reducing mortality, interventions should be aimed at improving uptake of patients and targeting noncompliance, mainly for CRC screening, as this is the most widely practiced[15]. S

Abbreviations

AASLD: American Association for the Study of Liver Diseases
ACG: American College of Gastroenterology
AFP: Alphafetoprotein
ASGE: American Society for Gastrointestinal Endoscopy
BSG: British Society of Gastroenterology
CRC: Colorectal cancer
DCBE: Double contrast barium enema
FAP: Familial Adenomatous Polyposis
FH: Family history
FOBT: Faecal occult blood test
HCC: Hepatocellular carcinoma
HGD: High grade dysplasia
HNPCC: Hereditary non-polyposis colorectal cancer
LGD: Low grade dysplasia
OGD: Oesophagogastroduodenoscopy
PSC: Primary sclerosing cholangitis
WGO: World Gastroenterology Organization
WHO: World Health Organisation

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